**Exhibit B**

## Shieh-Newton, Terri M.

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|---|---|
| **From:** | Darren Flower [darren.flower@jenner.ac.uk] |
| **Sent:** | Monday, March 06, 2006 2:27 AM |
| **To:** | Shieh-Newton, Terri M. |
| **Subject:** | RE: |

Hi,

There are no reliable ways of predicting T cell epitopes directly. Obviously, that hasn't stopped people from trying and reporting success, but our own work in this area indicates it is not possible. The best we have managed is a 75% success rate. The only real way is to predict the MHC binders and then test them. Obviously for class I, you now have a range of 8-15 residues to look at, so even for a small peptide, like your one, it is still some effort. There are things one could do, but nothing is guaranteed.

If you want to give me a ring, my number is below.

BW

DRF

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http://www.jenner.ac.uk/groups/bioinformatics.htm

http://www.rscmodelling.org

-----Original Message-----
**From:** Shieh-Newton, Terri M. [mailto:TShieh-Newton@mofo.com]
**Sent:** 03 March 2006 17:57
**To:** Darren Flower
**Subject:** RE:

Hi Dr. Flowers:

Thanks so much for your response. I'm not patent busting but rather just doing some research (rather boring compared to patent busting!).

I apologize for not being more clear in my first email -- I should frame my question differently. If I enter a peptide sequence, for example a string of 21 amino acids (ANNPLYKEATSTFTNTITYRGT), into your program, will your program tell me if there are any T cell epitopes in that 21 amino acid sequence? What about if there has been no publications that specifically report a T cell epitope that is contained in that 21 amino acid sequence?

I was reading your website and it says "all entries are from published experimentally determined data." My understanding is that T cell epitopes cannot be predicted just by looking at a specific sequence unless it has been experimentally tested and reported in a publication. That is, absent any reports by other investigators, there is not really a canonical sequence (like a TATA box or a polyA signal) that a scientist can use to determine whether a T cell epitope is contained within a peptide sequence just by looking at the sequence itself. The scientist would have to do some experiments, like making overlapping fragments that march down that 21 amino acid sequence and then test each of those peptide fragments for T cell proliferation (or cytokine production or some equivalent experiment) to determine if that particular peptide fragment is a T cell epitope.

Of course, if there is some publication that reports PLYKEATST is a T cell epitope, then everything is much easier. But the context that I am facing is that there are no other publications to rely upon and the scientist is just looking at the sequence itself and trying to determine if a portion of that sequence is a T cell epitope <u>without</u> doing any experiments and <u>without</u> the guidance of any publications.

If it's easier to discuss this over the telephone, please let me know and I can give you a call.

Thank you so much for your assistance.

Kind regards,
Terri


-----Original Message-----
**From:** Darren Flower [mailto:darren.flower@jenner.ac.uk]
**Sent:** Friday, March 03, 2006 3:00 AM
**To:** Shieh-Newton, Terri M.
**Subject:** RE:

Hi,

Thanks for your message. Since you work for a law firm, can I assume that you are interested in patent-busting?

I am not sure I really understand what you mean, but I think the answer to your question depends on what you mean by "epitope" and "peptide sequence".

T cell epitopes arise when a TCR recognizes a MHC-peptide complex. MHCs are of two types: class I (typically short peptides which bulge in the middle) and class II (longer peptides of which only a 9-11 region is involved in recognition). Obviously all only some residues are involved in recognition by the TCR.

If what you are really after is which regions in a whole protein sequence are epitopes this is a research question of some magnitude. There are lots of servers which will do this including ours:

www.jenner.ac.uk/mhcpred

www.jenner.ac.uk/epijen

3/14/2006

If you could clarify what you are after, I am sure I can offer some more assistance.

BW

DRF

-----Original Message-----
**From:** Shieh-Newton, Terri M. [mailto:TShieh-Newton@mofo.com]
**Sent:** 03 March 2006 01:37
**To:** Darren Flower; Helen McSparron
**Subject:**

Dear Dr. Flowers and Dr. McSparron:

I have a few questions about your AntiJen website. I am interested in using it to search for T cell epitopes in a specified peptide sequence. However, I am not sure if there has been any publications that clearly identifies which residues within the peptide sequence are T cell epitopes. In the absence of any publications that confirms the existence of T cell epitopes, can your website prgoram tell me if T cell epitopes exist if I enter a string of amino acid sequences into the search window?

Thank you so much for your time and assistance.

Kind regards,
Terri

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